Honey as a wound dressing treatment for odontogenic cutaneous fistula resulted from mandibular abscess

Madu sebagai perawatan pembalut luka untuk fistula kutaneus odontogenik akibat abses mandibula

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ABSTRACT
Odontogenic cutaneus fistula (OCF) arises as a sequel of bacterial invasion of the tooth. Evidence from animal studies and several trials suggests that honey has a potential role in the field of tissue engineering and regeneration. This article describes the management of OCF due to left mandibular abscess using honey as a wound dressing treatment. A 29-year-old woman was referred to Hasanuddin University Dental and Oral Hospital for evaluation of a painful left facial swelling with spontaneous purulent drainage and limited mouth opening. The patient had a history of recurrent toothache since 10 days before. The patient was admitted to the hospital and a tooth extraction was performed under local anaesthesia. The infected facial fistula was treated using honey as a wound dressing. After 12 weeks, tissue granulation and epithelisation were observed and the wound size was significantly reduced. It was concluded that the OCF management caused by mandibular abscess included observation and closed care, antibiotic therapy, surgical intervention, and honey as wound dressing.
Keywords: honey, mandibular abscess, odontogenic cutaneous fistula, wound healing

ABSTRAK
Fistula kulit odontogenik (FKO) muncul sebagai kelanjutan dari invasi bakteri pada gigi. Bukti dari penelitian pada hewan dan beberapa uji coba menunjukkan bahwa madu memiliki peran potensial dalam bidang rekayasa dan regenerasi jaringan. Artikel ini menjelaskan tatalaksana FKO akibat abses mandibula kiri dengan menggunakan madu sebagai perawatan pembalut luka. Seorang wanita usia 29 tahun, dirujuk ke Rumah Sakit Gigi dan Mulut Universitas Hasanuddin, untuk evaluasi pembengkakan wajah kiri yang menyakitkan dengan drainase spontan bernanah dan bukaan mulut terbatas. Pasien memiliki riwayat sakit gigi berulang sejak 10 hari sebelumnya. Pasien dirawat di rumah sakit dan dilakukan pencabutan gigi dengan anestesi lokal. Fistula wajah yang terinfeksi dirawat dengan menggunakan madu sebagai pembalut luka. Setelah 12 minggu, terlihat granulasi jaringan dan epitelisasi serta ukuran luka yang mengecil secara signifikan. Disimpulkan bahwa tatalaksana FKO yang diakibatkan oleh abses mandibula meliputi observasi dan perawatan tertutup, terapi antibiotik, intervensi bedah, dan madu sebagai pembalut luka.
Kata kunci: madu, abses mandibula, fistula kutaneus odontogenik, penyembuhan luka
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INTRODUCTION

A fistula is an abnormal pathological pathway between two anatomic spaces or a pathway that leads from an internal cavity or organ to the surface of the body. An odontogenic cutaneous fistula (OCF) is a pathologic communication between the cutaneous surface of the face and the oral cavity.[1] OCF or sinus is an uncommon, but well documented condition, which is often initially misdiagnosed as a sole cutaneous lesion and inappropriately treated.[1,2] An extraoral opening is the OCF, which usually arises as a sequel to bacterial invasion of the dental pulp through a breach in the enamel and the dentine by a carious lesion, trauma, or other causes.[3] If treatment is not initiated at this stage, the pulp becomes necrotic, and infection spreads beyond the confines of the tooth into the periradicular area, resulting in apical periodontitis. After affecting periapical tissue, this infection follow paths of lower resistance to drain purulent material.[3,4] The inflammatory process leads to bone resorption that subsequently dissects along the path of least resistance and erupts through skin where the discharge of purulent exudate flows through tissues and structures along paths of least resistance.[3,5]

Honey is a natural product made from the nectar of flowers by honey bees and has over 200 compounds in it, including sugars, water, organic acids, minerals and polyphenols.[6] Honey has been used as a wound treatment by indigenous cultures around the globe for thousands of years. Archeological findings and early written works indicate that wounds were treated with honey by the ancient Egyptians, Greeks, and Romans, among others.[7] There were in vitro and in vivo evidence supports this resurgence, demonstrating that honey debrides wounds, kills bacteria, penetrates biofilm, lowers wound pH, reduces chronic inflammation, and promotes fibroblast infiltration, among other beneficial qualities. Given these results, it is clear that honey has a potential role in the field of tissue engineering and regeneration,[6,7] so in this case honey is used as a wound dressing treatment for OCF resulted from mandibular abscess.

CASE

A 29-years-old female with no known co-morbidity, was referred to Oral and Maxillofacial Surgery Department, Oral and Dental Hospital of Hasanuddin University, in Makassar City regarding of painful facial swelling with open infected wound on the left cheek and limited opening of mouth. During history taking, the patient stated that she has recurrent toothache 10 days priorly then followed by facial swelling with pain and fever. The pa-

Figure 1a,b,c Marked facial swelling with an obvious sinus tract, **d** open sinus tract with pus actively discharged.

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tient had given antibiotic and analgetic per oral, but the swelling gradually grew larger and sinus tract was formed on her left cheek. At physical examination, marked swelling of the left face that extended to submandible and an obvious cutaneous fistula with pus discharge were present (Fig.1a,b,c).

On extraoral examination, facial swelling with 8x6x3 cm in size and a fistula on parotideamasseterica region with skin opening 3x4x1.5 cm in size with reddish, irregular border, and pus actively discharged was observed (Fig.1d). On palpation, the swelling were fluctuated and moderate pain. Mouth opening was only 2 cm. Intraorally, perforated profunda caries of tooth 38 and gangrene radix of teeth 27 and 36 was noted. There was elevated on left buccal vestibulum.

A head and neck CT-scan revealed soft tissue defect with wide swelling in left masticator, a part of salivary gland, and submandibular space with cervical enlargement of diffuse gland that suggested inflammation/infecfection process (Fig.2a).

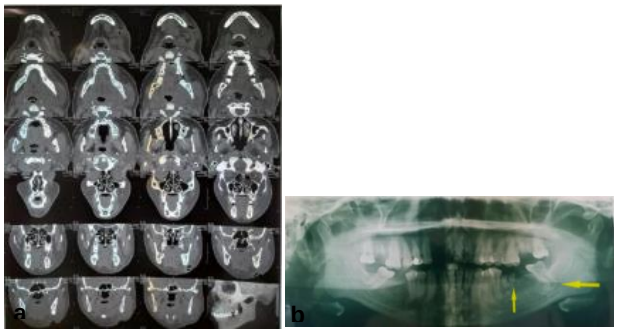

Figure 2a Head and neck CT-scan, **b** OPG of the patient; arrow indicate radiolucency around the apex of lower left first molar and third molar.

An OPG x-ray showed lower left third molar with profunda caries and periapical radiolucency. There were periapical radiolucencies around 27 and 36 region (Fig.2b). Routine blood laboratory tests result showed white blood cell count was 10.08 x 103/µL and hemoglobin (Hb) was 11.8 g/dL, that means the patient was leukocytosis and anemia. The patient was diagnosed as buccal abscess that spreading to submandible with OCF on the left cheek secondary to chronic periradicular periodontitis of teeth 36 and 38.

Then the patient was hospitalized with intravenous antibiotic theraphy (combination of aerob and anaerob) and analgetic for 3 days. Surgical extractions of teeth 38, 36, and 27 followed by wound cleaning of extraoral fistula wasperformed on local anesthesia (Fig.3a). The extraoral fistula spooled using povidone iodine 10% solution and bandaged using steril gauze with pressure. The steril gauze that smeared with povidone iodine 10% were changed every day.

Figure 3a Post surgical extractions of lower left first and third molar**, b** third day of treatment; pus discharge and edema was decreased with slightly active bleeding from the wound.

On the third day edema and pus were decreased with slightly active bleeding from the wound (Fig.3b). After spooling with saline solution, honey was applied on the wound. Honey used in this case was pure honey taken from the nectar of kapok flowers (Nusantara®, Jakarta, Indonesia). Wound dressings used were sterile gauze that had been smeared with honey. Wound care was performed every day and evaluated every 2 weeks to assess the signs of infection and the healing process of the wounds. The patient was discharged from hospital 3 days after surgical extractions with oral antibiotic theraphy.

After two weeks of honey dressing treatment, wound size was decreased to 1.5x2.5 cmx0.4 cm with muscle base, irregular edges, rising granulation tissue covering the muscle, and epithelialization at the wound edges. Edema, active bleeding, and pus were no longer found (Fig.4a). After 4 weeks of honey dressing treatment, muscle tissue was at base of wound base with rising granulation. Wound size was 0.5 cmx2 cm (Fig.4b). After 12 weeks, the wound was almost completely covered by healthy skin tissue and epithelialization with scab on the center of wound (Fig.4c). The scar was planned for repair of skin surgery with rotational flap.

Figure 4a The wound after 2 weeks of treatment, neither edema, active bleeding, and pus were found; **b** after 4 weeks of honey dressing, wound size was gradually smaller; **c** after 12 weeks of honey dressing, the wound almost completely recovered.

DISCUSSION

Odontogenic infections can be treated surgically or non-surgically. The OCF are one of the manifestations of chronic dental infections that provide a path for drainage of pus and infection.[4] Total elimination of the infectious focus and causative agent is essential for the successful treatment of fistulas, especially when they occur extraorally as observed in this case. In study reported by Guevara-Gutierrez *et al.* mentioned that 40 cases OCF were (53%) women and 35 (47%) were men, contrary to study by Saied and Al-Kinani where men predominated the cases (60%) more than women (40%). The most affected group of age reported by Guevara-Gutierrez et al was 51 years-old and over, while in study by Saied and Al-Kinani was 16-30 years-old.[3,8] In our case, the patient was 29 years-old female.

With respect to the location on the skin, Guevara-Gutierrez *et al*. mentioned that the most frequent location for OCF was the mandible angle 36% (27 cases), a frequency similar to 32.4% (11 cases) reported by Lee et al., or the 80% mentioned by Sotiropoulos and Farmakis.[2,3,5] Samir et al, mentioned that the classic lesion is a smooth, symmetric, erythematous nodule, up to 20 mm

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in diameter, with or without drainage, and presenting skin retraction secondary to healing.[3] However, in this case it was observed an open wound with necrotic tissue and pus actively discharged.

OCF, as one type of wound, is a disruption of the continuity of a tissue structure that causes destruction of tissue, disruption of blood vessels, and extravasation of blood constituents and hypoxia. Healing of acute wounds, triggered by tissue injury, consists of overlapping and highly coordinated phases of hemostasis, inflammation, proliferation and remodeling, resulting in scar formation.[10,11] Basically, wound healing is the result of interactions among cytokines, growth factors, blood and cellular elements, and the extracellular matrix.[9-12]

Conservative methods of wound care include the use of standard wound dressings, management of underlying problems (such as hyperglycemia), debridement of dead tissue, restoration of adequate tissue perfusion, limitation of pressure at the wound site, and control of infection.[9,13]

The composition of honey is variable, depending primarily on the floral source. Honey is a viscous, supersaturated sugar solution derived from nectar gathered and modified by the honeybee, *Apis mellifera*. Honey contains approximately 30% glucose, 40% fructose, 5% sucrose, and 20% water, as well as many other substances, such as amino acids, vitamins, minerals and enzymes.[14] Many studies have shown that honey has debridement effect which chemically accelerates the wound healing process. In vitro and in vivo evidence shows that honey eliminates bacteria, resolves inflammation, has anti-oxidants properties, and can be used as a wound dressing to promote rapid and improved healing.[6,7,9,15] Honey may positively influence 3 phases of wound healing (inflammatory, proliferative, and remodeling), including immunologic modulation via increased production of cytokines, as well as promotion of tissue granulation and epithelialization.[9,13-15]

Various studies revealed that the healing effect of honey could be classified by its antibacterial, anti-inflammatory, antioxidant, and debriding action properties of its components.[15-17] The beneficial role of honey is attributed to its antibacterial property with regards to its high osmolarity, acidity (low pH) and content of hydrogen peroxide (H_2O_2) and non-peroxide like methylglyoxal (MGO).[7,9,15-17] Various studies has been conducted with standardized to be equivalent to 12-16% phenol of honeys which has been demonstrated to be effective against several human pathogens and reported minimum inhibitory standard for a range of species of bacteria present in infected wounds: *Escherichia coli*, *Enterobacter aerogenes*, *Salmonella typhimurium*, *S.aureus*, various coagulase-negative *Staphylococci*, various species of *Enterococci*, *Pseudomonas aeruginosa*, *Klebsiella oxytoca*, *Streptococcus mutans*, a pathogen involved heavily in dental caries, and a range of anaerobes.[16-19] The antibacterial agent in honey is generated by glucose oxidase, an enzyme from the bee crop that slowly breaks down glucose into gluconic acid, which lowers the pH of honey, and hydrogen peroxide which helps kill bacteria.[7,9,17] Glucose oxidase is inactive under the low level of free water present in honey, but becomes active if the honey becomes diluted, as with wound exudate.[16,17] In a wound site, the lower pH of honey (3.5-4) reduces protease activity, increases oxygen release from Hb, and stimulates the activity of macrophages and fibroblasts, while the hydrogen peroxide content sterilizes the wound and stimulates vascular endothelial growth factor (VEGF) production.[7] It also found that solutions of high osmolarity, such as honey, glucose, and sugar pastes, inhibit microbial growth because the sugar molecules tie up water molecules so that bacteria have insufficient water to grow.[9,16]

Laboratory studies have revealed that the honey is effective against methicillin-resistant *S.aureus* (MRSA), ß-haemolytic streptococci and vancomycin-resistant *Enterococci* (VRE).[16] Honey acts to stop the growth of microbes with its high sugar content and low pH (bacteriostatic action) and kill bacteria via its antibacterial factors, especially hydrogen peroxide.[15-18] The antibacterial property of honey has been the focus regarding its use in wound healing; however, it is important to realize that honey is not a substitute for antibiotics.[19]

Honey can remove the bacteria that causes inflammation. Molan and Rhodes published a review article covered various works that has demonstrated immunestimulatory activity of honey on leukocytes causes the production of cytokines, which lead to the stimulation and growth of cells.[17] Al-Waili et al mentioned in their review that honey can lower plasma prostaglandin concentrations in normal individuals. Its inhibitory effect was increased with time. The site of actions could be either at COX-1 or COX-2, or both.[9] The anti-inflammatory action of honey reduces edema and exudates, which can subsequently improve wound healing and also reduces pain caused by pressure on nerve endings and reduces the amount of prostaglandin produced in inflammatory process. Honey also stimulates the angiogenesis, granulation and epithelialisation, which helps speed up the healing process. Honey can trigger the sequence of events to enhance angiogenesis and proliferation of fibroblasts and epithelial cells by producing certain growth factors like tumor necrosis factor (TNF-alpha).[15,17]

Many studies have shown that honey has debridement effect which chemically accelerates the wound healing process. Honey also has an anti-inflammatory effect which reduce edema and exudate, provide a calming effect, and minimize the formation of scar.[9,17] It is suspected that the anti-oxidant components of honey such as flavonoids, monophenolics, polyphenols, and vitamin C, high osmotic pressure in honey, as well as the hydrogen peroxide composition are related to these findings.[15-17] High osmolarity can draw the water from the wound base and creating an outflow from the lymph, thus reducing tissues edema around the wound.[9,15-17] Hydrogen peroxide stimulates the activity of the protease and improves plasmin activity in digesting fibrin on the surface of the wound.[5,7,16,18]

A systematic review by Jull *et al*, mentioned various trials were applying honey on the wound as a honey im-

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pregnated gauze dressing, as a honey impregnated alginate dressing, as honey spread between gauze, and as topical honey covered with either a film dressing or with gauze.[14] In our case, honey was applied as topical honey covered with gauze and replace every day. As mentioned by Minden-Birkenmaier and Bowlin, a high concentration of honey can be applied topically to the wound to destroy the biofilm and eradicate the bacteria. After the infection has been eliminated, a tissue engineered template can be applied which releases lower levels of honey to reduce inflammation and aid in tissue regeneration, without causing cytotoxicity.[7]

In our case, honey has proven the ability to stimulate granulations and epithelializations in OCF treatment with no reported side effects. So, it is concluded that management for OCF resulted from mandible abscess include closed observation and treatment, antibiotic therapy, surgical intervention, and honey as a wound dressing. With antibacterial, anti-inflammatory, antioxidant, immunostimulatory effect, and other properties of honey, it is recommended to use honey as a biologic wound dressing that work in concert to expedite the healing process.

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